ANTITHROMBOTIC EFFICACY OF CONTINUOUS EXTRADURAL ANALGESIA AFTER KNEE REPLACEMENT

L. N. JØRGENSEN, L. S. RASMUSSEN, P. T. NIELSEN, A. LEFFERS AND E. ALBRECHT-BESTE

SUMMARY

We have studied the effect of extradural analgesia on postoperative venous thrombosis in patients undergoing knee arthroplasty. Forty-eight patients were allocated randomly to receive either general anaesthesia or extradural analgesia with local anaesthetics for 3 days. All patients wore compressive elastic stockings and no anticoagulant drugs were administered. Bilateral venography was performed 10 days after surgery. Continuous extradural analgesia did not impede mobilization of the patients. One case of non-fatal pulmonary embolism occurred in a patient who received general anaesthesia. The use of continuous extradural analgesia resulted in a significant difference in the total incidence of deep vein thrombosis (18% compared with 59% after general anaesthesia (P = 0.02)). The incidence of calf vein thrombosis was 12% compared with 45% after general anaesthesia (P = 0.05).

KEY WORDS

Studies on patients undergoing knee arthroplasty suggest that this group of patients has a high incidence of postoperative deep vein thrombosis (DVT) [1–3]. Several investigations have shown that the incidence of DVT (demonstrated by venography) following hip surgery is reduced when the operation is performed under lumbar extradural or subarachnoid analgesia [4–7].

In the present study we have examined the effect of continuous lumbar extradural analgesia (EA) on the incidence of DVT after knee arthroplasty.

PATIENTS AND METHODS

The study was approved by the regional Ethics Committee and patients undergoing elective knee arthroplasty (primary or revision) gave informed consent to take part in the study. We excluded patients receiving antithrombotic medication, premenopausal women and those with a history of venous thromboembolic disease or allergy to radio-opaque contrast media. The patients were allocated randomly to either extradural anaesthesia (EA) or general anaesthesia (GA).

We considered 58 consecutive patients for inclusion in the study; three suffered from medical diseases which were contraindications to GA, and seven refused to enter the study. Hence, 48 patients were studied initially: 24 EA and 24 GA. Nine patients did not complete the study: five because of insufficient venography (technical problems, refusal by patient); two in whom Dextran 500 ml i.v. was administered during the operation; one in whom EA was insufficient and to whom GA was administered; and one subarachnoid anaesthesia. Thus data were obtained on 39 patients (table I).

All patients were premedicated with diazepam 0.3 mg kg⁻¹ orally.

Continuous extradural analgesia

Before anaesthesia, all patients received an i.v. infusion of saline 1000 ml. With the patient in the horizontal lateral position, we administered a test dose of 2% mepivacaine 3 ml with adrenaline

L. N. JØRGENSEN*, M.D., L. S. RASMUSSEN, M.D. (Department of Anaesthesia); P. T. NIELSEN, M.D. (Department of Orthopaedic Surgery); A. LEFFERS, M.D., E. ALBRECHT-BESTE, M.D. (Department of Radiology); Hillerød Central Hospital, DK-3400 Hillerød, Denmark. Accepted for Publication: July 2, 1990.

*Present address, for correspondence: Department of Surgical Gastroenterology, Hvidovre Hospital, DK-2650 Hvidovre, Denmark.
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TABLE I. Characteristics of the 39 randomized patients completing the study. EA = Extradural analgesia; GA = general anaesthesia

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EA (n = 17)</th>
<th>GA (n = 22)</th>
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<tbody>
<tr>
<td>Age (yr) (median (range))</td>
<td>70.5 (52-87)</td>
<td>64.0 (38-85)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>4/13</td>
<td>7/15</td>
</tr>
<tr>
<td>Body mass index (kg m⁻²) (median (range))</td>
<td>27 (19-32)</td>
<td>27 (21-46)</td>
</tr>
<tr>
<td>Cardiac decompensation or arrhythmia</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

followed by 2% mepivacaine 8–15 ml through a lumbar extradural catheter with its tip located approximately at the level of the third lumbar vertebra. If necessary, small doses of diazepam, fentanyl or both were given during surgery.

After operation, 0.25 % bupivacaine 5 ml h⁻¹ was infused through the extradural catheter by infusion pump (Perfusor, Secura, B. Braun). This dose was adjusted to achieve pain relief corresponding to a sensory block from L1-2 to L5/S1. In order to avoid interfering with routine mobilization, muscle function of the quadriceps of the non-operated leg was assessed frequently, and preserved by adjustment of the dose. This regimen was maintained until the third day after operation in 15 patients. The extradural catheter was removed on the second day in two patients in whom the neural block was insufficient.

General anaesthesia

Thiopentone 3–5 mg kg⁻¹ was used for induction of anaesthesia. Before tracheal intubation, fentanyl 5 μg kg⁻¹ and pancuronium 0.1 mg kg⁻¹ were administered. Following tracheal intubation, the lungs were ventilated with 66% nitrous oxide in oxygen and diazepam 0.2 mg kg⁻¹ administered i.v. Fentanyl was given intermittently during surgery in doses of 100 μg i.v. when appropriate, and muscle relaxation was maintained by intermittent administration of pancuronium 1–2 mg i.v. Residual neuromuscular block was antagonized with glycopyrroline 0.4 mg and pyridostigmine 10 mg. For postoperative pain relief the GA patients received i.m. injections of ketobemidone 5.0–7.5 mg on demand, and, when tolerated, ketobemidone 5–10 mg and paracetamol 1 g orally on demand.

Peri- and postoperative procedures

A standardized technique was used for all operations, with the patient in the supine position. An inflatable femoral tourniquet was applied after elevation of the leg. Before removal of the tourniquet a compressive elastic bandage was placed around the lower leg.

Anticoagulant prophylactic drugs were not administered, but patients wore thigh-length compressive elastic stockings (Comprinet, Beiersdorf) on the contralateral leg from before operation and a below-knee stocking on the other leg from the morning on the first day after operation. The stockings were not removed until the patient was ambulant.

All patients followed the same physiotherapy regimen with quadriceps exercises and active knee mobilization on the first day, and walking with full weight bearing on the second day after operation.

The volume of blood loss in the suction drains was assessed daily. In addition, the patients were examined routinely for signs or symptoms of DVT, pulmonary embolism, or both; if necessary, venography, ventilation-perfusion lung scan, or both, were carried out.

Bilateral ascending venography including exposure of the common and external iliac veins was performed 9–11 days after surgery as described by Rabinov and Paulin [8]. Iohexol (Omnipaque) 240 mg ml⁻¹ was used as contrast medium.

The venograms were scrutinized by the same two experienced radiologists, who were unaware of the anaesthetic used. Diagnosis of DVT required a constant luminal defect in the deep veins on at least two projections visible to both radiologists. Defects apparent only in the communicating veins were not considered. The endpoints sought were either absence of DVT based on bilateral venography, or occurrence of DVT based on uni- or bilateral venography.

Statistics

The Mann–Whitney two-sample rank sum test was used for comparison of unpaired data between two groups. The difference between two rates was evaluated by Fischer's test. P < 0.05 was regarded as statistically significant.

RESULTS

The groups were similar with respect to age, sex, body mass ratio, cardiac disease, presence of varicose veins (table I) and perioperative characteristics (table II). The total blood loss in
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TABLE II. Peri- and postoperative characteristics of 39 patients completing the study (median (range))

<table>
<thead>
<tr>
<th></th>
<th>EA (n = 17)</th>
<th>GA (n = 22)</th>
</tr>
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<tbody>
<tr>
<td>Duration of tourniquet inflation (min)</td>
<td>80 (55–100)</td>
<td>83 (55–105)</td>
</tr>
<tr>
<td>Total volume in drains (ml)</td>
<td>650 (340–1845)</td>
<td>950 (195–3275)</td>
</tr>
<tr>
<td>Transfusion requirements (number of packages)</td>
<td>0 (0–2)</td>
<td>0 (0–5)</td>
</tr>
</tbody>
</table>

TABLE III. Incidence and location of DVT, and incidence of pulmonary embolism. Location refers to most proximal extension of the thrombus

<table>
<thead>
<tr>
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<th>EA (n = 17)</th>
<th>GA (n = 22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calf vein</td>
<td>2</td>
<td>10</td>
<td>0.05</td>
</tr>
<tr>
<td>Popliteal veins</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Femoral veins</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>DVT (total)</td>
<td>3</td>
<td>13</td>
<td>0.02</td>
</tr>
<tr>
<td>DVT on non-operated side</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Symptomatic DVT</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>1</td>
<td></td>
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</tbody>
</table>

the drains did not differ significantly between the groups (P = 0.4).

Extradural analgesia was continued for at least 2 days after operation in the majority of the EA patients and no serious complications were observed.

The distribution and location of DVT in the two groups of patients are illustrated in table III. All patients with involvement of the popliteal or femoral veins also had venographic filling defects in calf veins. The use of EA was associated with a 17% incidence of DVT (95% confidence limits 2–36%), which was significantly less than the 59% incidence (36–79%) found in the GA group (P = 0.02). Only thrombotic lesions exclusively involving the lower leg veins were significantly fewer (P = 0.05). Only two cases of symptomatic DVT occurred, both in the GA group, and the thrombi were confined to the calf. Two patients had DVT only in the non-operated leg. One case of non-fatal pulmonary embolism was verified 5 days after operation in a patient in the GA group, in whom thrombotic lesions involved only the lower leg veins.

DISCUSSION

Several studies have shown that, following knee arthroplasty, the incidence of DVT (assessed by venography) is 40–80%, if prophylaxis has not been administered [1–3]. Most patients in these studies underwent surgery under GA. Despite the high risk of development of postoperative DVT, few randomized trials have been carried out using objective outcome measures to investigate prophylactic regimens for these patients. The incidence of DVT was reduced significantly in patients treated with intermittent pneumatic compression devices [9, 10], high dose aspirin [10], low dose warfarin [11], or antithrombin III combined with low dose heparin [12]. No effect was detected following use of either continuous passive knee motion [1] or low dose aspirin [10].

The present study has demonstrated that the use of continuous EA with local anaesthetics significantly reduced the incidence of calf vein thrombosis in patients undergoing knee arthroplasty. It is generally considered that thrombi located in the popliteal or femoral veins possess a higher embolic potential; the results of this study suggested that prevention of larger vein involvement might also be important, although this was not statistically significant. Assuming a 5% level of significance and an 8% minimum detectable difference of the incidence of proximal DVT, the statistical risk of failure to detect a real difference between the groups (type II error) was greater than 90%, because of the small number of patients studied. The typical distribution of the thrombi, with a predominance of calf vein lesions, is similar to that of other venographic studies [2, 3]. Similarly, we report a comparable incidence of symptomatic pulmonary embolism of 2%. When pulmonary scans were performed routinely after surgery, Stulberg and colleagues reported a 7% incidence of pulmonary embolism [12]. In other studies using bilateral venography, there is evidence of an antithrombotic effect from the use of regional lumbar anaesthesia in patients undergoing elective [4, 5, 7] and acute hip surgery.
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However, Modig and colleagues did not find a significant reduction in the incidence of total DVT [4, 5], and the patients in the study by Thorburn, Louden and Vallance were not randomized [7]. Interestingly, the incidence of postoperative pulmonary embolism assessed by ventilation-perfusion scintigraphy was reduced significantly in patients undergoing hip surgery under regional anaesthesia compared with GA. Modig’s group also found that the postoperative incidence of pulmonary embolism assessed by ventilation-perfusion scintigraphy was reduced significantly in patients undergoing hip surgery under regional anaesthesia compared with GA [4, 5].

There may be several mechanisms to account for the prophylactic effects of EA. Regional lumbar block involving the L1 and L2 spinal nerves increases blood flow in the lower limbs [13]; there is also evidence that platelet aggregation and blood viscosity are reduced [14]. There are data suggesting that inhibition of coagulation and enhancement of fibrinolysis is induced by EA [15, 16], but these findings were not reproduced in a study by Rem and colleagues, who suggested that postoperative enhancement of coagulation, and impairment of fibrinolysis are regulated by factors other than neurogenic and adrenal [17].

Because of the use of tourniquets, it is clear that the protective role of EA against DVT in knee arthroplasty is not mediated by enhanced intraoperative blood flow. It is not clear if the antithrombotic effect of EA is mediated during or after surgery, but we used a 3-day duration of sympathetic block of vessels of the lower legs as most thrombi develop during this period [18]. We have no data to determine if a shorter regimen of EA would prove as beneficial.

The use of a tourniquet was postulated to reduce the incidence of DVT, but that study was uncontrolled [19]. Ischaemia caused by a tourniquet enhances local fibrinolysis, probably by release of tissue plasminogen activator from the vessel wall [19]. However, increased thrombolytic activity is short lived, and decreases to preoperative values within 30 min after deflation of the tourniquet. In two trials using well-matched control groups there was no difference in the incidence of DVT after surgery on the lower extremity with and without the use of a tourniquet [20].

Blood loss following various surgical procedures (hip [4, 5], hysterectomy, lower limb vascular surgery or amputation, and prostatectomy [21]) is decreased after lumbar regional anaesthesia compared with GA. In the present study, there was no significant difference in drainage, even though EA was prolonged for several days into the postoperative period.

ACKNOWLEDGEMENT

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REFERENCES


